Appendix C

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Eivind Per Thor Straten	Examiner:	Marianne DiBrino, Ph.D.
Serial #:	10/715,417	Group art unit:	1644
Filed:	19 November 2003	Docket:	60820.000004
Title:	SURVIVIN-DERIVED PEPTIDES AND USE THEREOF		

Commissioner For Patents

P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132 BY Dr. MADS HALD ANDERSEN

Sir:

1. I, Mads Hald Andersen, residing at Hegnsvej 61, Dk-2850 Naerum, Denmark, do state and declare as follows:

2. I am one of the two named inventors of the above-captioned patent application. As of December 8th 2003 I have assigned all of my right, title and interest to the invention to the proprietor, Survac ApS, a company of which I was part owner. As of January 6th 2006, Survac ApS was acquired by Merck KGaA of Frankfurter Str. 250, 64293 Darmstadt, Germany. At present, I am not in any way associated with the present proprietor of the application and there are no residual (PECUNIARY) rights to the invention remaining with me. Furthermore, I have no financial interest (e.g. stocks) in the present proprietor of the patent.

3. I have been informed that on March 23, 2007 the United States Patent and Trademark Office issued an Office Action in regard of the above-captioned application. I have further been informed that one of the issues raised in said Office Action relates to the following two publications:

MHA 15/9-07

Andersen *et al.*, Identification of a cytotoxic T lymphocyte response to the apoptosis inhibitor protein survivin in cancer patients, Cancer Res. 61, 869-72, 2001

Andersen *et al.* Spontaneous cytotoxic T-cell responses against survivin-derived MHC class I-restricted T-cell epitopes *in situ* as well as *ex vivo* in cancer patients, Cancer Res. 61, 5964-8, 2001

In the following I shall provide information on the contribution of each of the non-inventor and inventor authors to the two publications:

Cancer Research 61, 869-72, 2001:

Authors: Mads Hald Andersen, Lars Østergaard Pedersen, Jürgen C. Becker, and Per thor Straten

The study and the suggestion to use survivin peptides for immunotherapy of cancer as disclosed in the publication were based on an idea from Mads Hald Andersen and on analysis and interpretation of experimental data by Mads Hald Andersen and co-inventor and co-author Per thor Straten. Survivin peptides were designed by Mads Hald Andersen who also performed the research and drafted the manuscript.

Lars Østergaard Pedersen was listed as co-author by courtesy as he was expected to generate HLA/peptide complexes at a later time (see below)

Jürgen C. Becker edited the manuscript and was expected to perform in situ stainings at a later time (see below)

Cancer Research 61, 5964-5968, 2001.

Authors: Mads Hald Andersen, Lars Østergaard Pedersen, Barbara Capeller, Eva-Bettina Bröcker E-B, Jürgen C. Becker, and Per thor Straten.

The study and the suggestion to use survivin peptides for immunotherapy of cancer as disclosed in the publication were based on an idea from Mads Hald Andersen and further based on analysis and interpretation of experimental data by inventor Mads Hald Andersen and co-inventor and co-author Per thor Straten. Survivin peptides were designed by Mads Hald Andersen who also performed the research and drafted the manuscript.

Per thor Straten: analyzed and interpreted data and edited the manuscript

Lars Østergaard Petersen: performed technical work: he generated HLA/peptide complexes for further use.

Jürgen C. Becker: edited the manuscript, performed technical work, including *in situ* stainings.

MAH 15/5-07

Barbara Capeller contributed blood samples from breast cancer patients

Eva-Bettina Bröcker was listed as co-author merely by courtesy to acknowledge her capacity as head of Department of Dermatology, Würzburg University, Germany

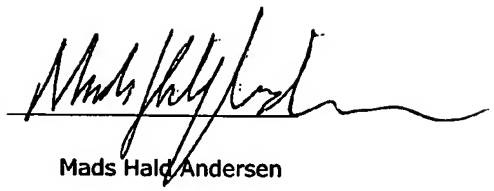
4. I have further been informed that, in response to a requirement for election of species, the above-captioned application is directed to an epitope_peptide selected from the peptides set forth in SEQ ID NO: 1 (Sur6), SEQ ID NO: 4 (Sur1L2), SEQ ID NO: 5 (Sur1M2) and SEQ ID NO: 14 (Sur4). One particular claim is directed to a composition comprising the peptide set forth in SEQ ID NO:14 and the peptide set forth in SEQ ID NO:36 (FTELTLGEF). The clinical relevance of using the Sur1M2 peptide in cancer immunotherapy is demonstrated in Example 5 of the application. It is my opinion that the clinical relevance of using the other peptide species in cancer therapy is supported by the fact that in relation to the subject survivin tumor associated-antigens it is not possible to identify a single dominant epitope peptide. In addition, the inclusion of more peptide species may provide for the targeting of multiple HLA alleles/molecules.

5. Additionally, I have been advised that the Office Action has cited a publication of Reker et al., Cancer Biology and Therapy, 3: 2, 173-179, 2004 for stating that "To date, it is not known whether survivin is indeed a tumor rejection antigen..." I am a named author on this scientific publication. This statement was presented in the discussion of the research data, not to express concerns with respect to the relevance of using survivin peptides in cancer immunotherapy, but merely to indicate that phase III clinical trials - the only firm proof that a vaccine works - had not yet been completed. The therapeutic trial experiments presented in Example 5 of the application is to me a sure indication of the clinical relevance of using survivin epitopes in immunotherapy and that survivin is involved in tumour immunity.

6. Finally, I have been informed that a further issue raised in the Office Action relates to the availability of the melanoma cell line, FM3. The cell line was originally described by Kirkin et al., Cancer Immunol Immunother, 41: 71-81, 1995 and is well recognised within the art. Additionally the cell line is included in the IPD-ESTDAB database at http://www.ebi.ac.uk/cgi-bin/ipd/estdab/print_cell.cgi?ESTDAB-007 and is available with no restrictions. The cell line is identified as ESTDAB-007 (FM3).

7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statement and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United State Code, and that such wilful false statements may jeopardize the validity of the application or any patent issued thereon.

15/1/07

Dated: 09/15/2007 Signature: 

month/day/year Mads Hald Andersen